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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/072,425	MOSER ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/6/02, 1/12/04, 3/29/04,1/3/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *3,8,19,29 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-7,9-18,20-28,30-39 and 41-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of the species, dendritic cells (DCs) of myeloid origin, in the paper filed 1/03/05, is acknowledged. Upon reconsideration, DCs of lymphoid origin are rejoined.

2. Claims 3, 8, 19, 29, and 40 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 1, 2, 4-7, 9-18, 20-28, 30-39, and 41-57 read on the elected invention and are being acted upon.

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

A) Uninitialed changes in the residence address of Inventor Lespagnard have been made.

B) It is noted that the declaration has not been dated by Inventor Velu. However, MPEP 602.05 states that a new declaration will no longer be required in instances wherein the date of execution has been omitted.

4. The specification is objected to. Specifically, "March 27, 2001" in the priority data at page 1 should be "March 27, 1998".

5. Applicant has claimed the benefit of priority to U.S. Application Nos. 08/414,480, 08/625,507, 09/025,405, and 09/049,502.

In the instant application the term "dendritic cell" (DC) has been defined twice. At page 4 the term is defined to include "all non-B cells present in purified or enriched preparations of dendritic cells." It is also noted that at page 4 the term is disclosed as being interchangeable with the term "dendritic-like cell." DC is also defined at page 11 as "an isolated dendritic cell or its dendritic progenitor." Note that the second definition, while at first seeming to narrow the scope of the first, does not actually indicate that any of the "non-B cells" of the page 4 definition are intended to be excluded. Indeed, the page 11 definition can be interpreted as broadening the scope of the term to include dendritic

progenitors not found in purified or enriched preparations. Accordingly, in the instant context, the term "dendritic cell" is considered to encompass all "non-B cells present in purified or enriched preparations of dendritic cells" as well as "dendritic progenitors" wherever they may be found.

Given the aforementioned definition of a DC the instant application cannot be granted the benefit of priority to the '480 parent application as said application does not disclose the broad definition of DC, i.e., "dendritic-like cells", found in the instant application. Additionally, the '480 application does not disclose DCs of lymphoid or myeloid origin, nor does it disclose a DC progenitor.

Regarding the '507 and '405 applications, at page 3, said applications disclose the broadly defined "dendritic-like cells" of the instant application. As the term "dendritic-like cell" is defined as being interchangeable with the term "dendritic cell", the instant application is granted the benefit of priority to the '507 application, i.e., a priority date of 3/29/96, with two exceptions. Withdrawn Claims 6, 17, 27, and 38 are drawn to DCs of lymphoid origin. Said DCs are not disclosed in the '507 nor '405 applications. Withdrawn Claims 8, 19, 29, and 40 are drawn to a DC progenitor. Said DC is not disclosed in the '507 nor '405 applications. Accordingly, said withdrawn claims are granted the priority date of the '502 application, 3/27/98.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1, 4, 5, 6, 7, 9, 10, 11, 15, 16, 17, 18, 20, 21, 22, 25, 26, 27, 28, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guo et al. (1994, IDS) in view of Sornasse et al. (1992).

Guo et al. teaches a method for producing a plurality of hybrids/hybridomas comprising a bone marrow derived antigen-

presenting B cell and a tumor cell (see particularly page 520, columns 2-3, 11.). The method comprises the providing of a tumor sample and an isolated autologous B cell, and the fusing of the cells with PEG to produce a plurality of hybrids/hybridomas (see particularly page 518, column 2). The reference teaches that the hybrids/hybridomas comprise cells that express both tumor-specific antigens and the machinery for antigen presentation, i.e., characteristics of both tumor cells and B cells (see particularly page 518, column 1), that said hybrids/hybridomas are useful for the induction of an anti-tumor response in that they reduce the number of tumor cells upon administration to a subject (see particularly page 518, column 3). The reference further teaches that the hybrids/hybridomas were selected on the basis of a tumor cell surface marker and a B cell surface marker (see particularly page 518, column 3).

The reference teaching differs from the claimed invention only in that it does not teach the use of a DC as the antigen presenting component of the hybrid.

Sornasse et al. teaches that, while both B cells and DCs are capable of inducing IL2 secretion *in vitro*, DCs induce a more vigorous response, including a Th1 response, *in vivo* (see particularly pages 16-17, Results). The reference teaches the superiority of DCs over B cells for *in vivo* use, "Our data emphasize the main role of DC in initiating primary responses in vivo" (see page 18, column 1). Note that the DCs of the reference comprise splenic DCs which would include bone marrow derived DCs, lymphoid DCs, and myeloid DCs.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce the hybrids/hybridomas of Guo et al., by the method of Guo et al., substituting a DC for the B cell in said hybrids/hybridomas, as taught by Sornasse et al. One of ordinary skill in the art at the time of the invention would have been motivated to make said substitution because, while both B cells and DCs are capable of inducing IL2 secretion *in vitro*, DCs induce a more vigorous response, including a Th1 response, *in vivo*, as taught by Sornasse et al. "Our data emphasize the main role of DC in initiating primary responses in vivo". Note that the additional limitations such as preparing a primary cell culture of the tumor cells comprises only an obvious and necessary step when said culture is not readily available as it was for Guo et al. Note, however, the BERH-2

tumor cells of Guo et al. derive from a hepatocarcinoma thus, said cells were previously the "primary culture" of tumor cells as set forth in the claims.

8. Claims 2, 12, 33, 42, 43, 44, 46, 47, 48, are rejected under 35 U.S.C. § 103(a) as being unpatentable over Guo et al. (1994, IDS) in view of Sornasse et al. (1992), as applied to Claims 1, 4, 5, 6, 7, 9, 10, 11, 15, 16, 17, 18, 20, 21, 22, 25, 26, 27, 28, and 29 above, and in further view of U.S. Patent No. 5,851,756.

Guo et al. and Sornasse et al. have been discussed, supra. The references differ from the claimed invention in that they do not teach the induction of DC characteristics before using said hybrids/hybridomas, nor the induction of said characteristics using GM-CSF.

The '756 patent teaches the induction of DC characteristics using GM-CSF (see particularly Example I). The reference further teaches that DC exist in relatively small numbers in blood, thus the induction of DC (and thus, DC characteristics) in GM-CSF before use provides a method to increase the number of said DCs (see particularly column 4, line 63 - column 5, line 9).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce the hybrids/hybridomas of Guo et al. and Sornasse et al., by the method of Guo et al., substituting a DC induced with GM-CSF before use, as taught by the '756 patent, for the B cell in said hybrids/hybridomas. One of ordinary skill in the art at the time of the invention would have been motivated to induce DC (and thus, DC characteristics) with GM-CSF before use because DC exist in relatively small numbers in blood, thus the induction of DC in GM-CSF before use provides a method to increase the number of said DCs, as taught by the '756 patent.

9. Claims 50-52, and 54-56 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Guo et al. (1994, IDS) in view of Sornasse et al. (1992), as applied to Claims 1, 4, 5, 6, 7, 9, 10, 11, 15, 16, 17, 18, 20, 21, 22, 25, 26, 27, 28, and 29 above, and in further view of U.S. Patent No. 5,637,483.

Guo et al. and Sornasse et al. have been discussed, supra. The references differ from the claimed invention in that they do

not teach the treatment of the hybrids/hybridomas with irradiation before using to prevent proliferation.

The '483 patent teaches the treatment of a tumor cell-containing anti-tumor vaccine with irradiation before using to prevent proliferation (see particularly column 3, lines 65-67 and column 14, lines 3-4).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce the hybrids/hybridomas of Guo et al. and Sornasse et al., by the method of Guo et al. and employ irradiation before using, as taught by the '483 patent. One of ordinary skill in the art at the time of the invention would have been motivated to treat the hybrids/hybridomas with irradiation before using to prevent proliferation, as taught by the '483 patent.

10. Claims 13, 14, 23, and 24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Guo et al. (1994, IDS) in view of Sornasse et al. (1992), as applied to Claims 1, 4, 5, 6, 7, 9, 10, 11, 15, 16, 17, 18, 20, 21, 22, 25, 26, 27, 28, and 29 above, and in further view of Reid et al.

Guo et al. and Sornasse et al. have been discussed, supra. The references differ from the claimed invention in that they do not teach the use of HAT for the killing of unfused drug-sensitive immortal tumor cells.

Reid et al. teaches the use of the HPRT gene to create a drug-sensitive cell for convenience of selection and killing employing multiple selectively toxic agents including HAT (see particularly page 4299, column 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce the hybrids/hybridomas of Guo et al. and Sornasse et al., by the method of Guo et al. employing the HPRT gene of Reid et al. One of ordinary skill in the art at the time of the invention would have been motivated to employ the HPRT gene in the hybrids/hybridomas given the teachings of Reid et al. that the introduction of the HPRT gene creates a drug-sensitive cell for convenience of selection and killing employing multiple selectively toxic agents including HAT.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 18-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically:

A) The "said drug" in Claims 13, 23, and 34 has no antecedent basis in Claim 10, 21, and 31, respectively.

B) In Claims 47-49, "GM-CSF IFN-γ" should be "GM-CSF, IFN-γ".

13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1, 2, 4-7, 9-18, 20-28, 30-39, and 41-57 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the recitation of:

A) The method of producing a fused cell product "for the reduction of the number of tumor cells in a patient", in Claims 1, 10, and 21.

B) The method of producing a fused cell product "using PEG", in Claims 9, 20, 30, and 41.

C) The method of producing a fused cell product comprising: "(b) analyzing tumor-associated antigens of said tumor sample, (c) providing an established cell line comprising immortal human tumor cells having at least one tumor-associated antigen in common with said tumor sample", in Claim 31.

Regarding A) and C), the specification does not disclose these limitations.

Regarding B), the specification teaches this limitation only in specific examples, e.g., the fusing of specific mouse or human cell lines, and not in the claimed generic context.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805 The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

3/15/04

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
August 08, 2003